

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Risk factors, risk stratification and risk-specific surveillance strategies after endovascular aneurysm repair: Study protocol for a Delphi study by the International Risk Stratification in EVAR (IRIS- EVAR) working group
AUTHORS	Antoniou, George A.; Schermerhorn, Marc L.; Forbes, Thomas; Cheng, Vincent; Antoniou, Stavros; Golledge, Jonathan; Verhagen, H; Torella, Francesco

VERSION 1 – REVIEW

REVIEWER	Shin, Seungwon Kyung Hee University
REVIEW RETURNED	17-Aug-2021

GENERAL COMMENTS	The manuscript has been clearly and sufficiently revised.
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REVIEWER	Khashram, M The University of Auckland Department of Surgery, Department of Vascular Endovascular and Transplant Surgery
REVIEW RETURNED	28-Aug-2021

GENERAL COMMENTS	Thank you again for the opportunity to review the revised manuscript by Dr G Antoniou et al. entitled "Risk factors, risk stratification and risk-specific surveillance strategies after endovascular aneurysm repair: Study protocol of the International Risk Stratification in EVAR (IRIS-EVAR) working group" resubmitted as a protocol for consideration by BMJ Open. The authors have revised the manuscript and considered the comments and suggestions accordingly. I have no further comments and wish them success with interesting project.
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REVIEWER	McConnachie, Alex University of Glasgow, Robertson Centre for Biostatistics
REVIEW RETURNED	06-Sep-2021

GENERAL COMMENTS	<p>There is very little in the way of statistics for me to comment on, but one thing that struck me was that the "Can't say" responses will be excluded from analyses, which is perfectly fine, but raises the question as to what happens if most people give this response. Is there a threshold for the number or proportion of definite responses that are required?</p> <p>Otherwise, my only comment is about the strengths and limitations section of the paper, which lists strengths, but no weaknesses. Surely there are some?</p>
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REVIEWER	Bismuth, Jean Houston Methodist Hospital, Vascular Surgery
REVIEW RETURNED	06-Sep-2021

GENERAL COMMENTS	<p>Although, I understand the importance of achieving a consensus report on EVAR, as I'm certain the authors are aware, this is a very complex problem with innumerable variables. It's complexity is really the driving obstacle here. I therefore call attention to the issue of selecting experts;</p> <p>1) The authors underline the need to ensure geographical, sex and age diversity, which is fine, but the complexity of this question is in my opinion linked to several areas of expertise; an explicit understanding of device mechanics, imaging tools (strengths & weaknesses), as well as fluid dynamics. As such it would be beneficial to understand the designation of "experts" in more detail.</p> <p>2) Given the potential benefits of such a paper, it would be beneficial to understand from the authors how they believe that the work will be able to forecast future solutions and how the work may be used to influence changes at the industry level.</p> <p>3) One of the most important elements in this analysis would be to be able to remove all industry bias from this analysis. All clinicians in this arena are tied to primarily one vendor, how is this bias being handled in the analysis? Do the authors feel that this is adequately accounted for?</p> <p>4) Have the authors considered also having a question for operative embolization of IMA/Lumbar branches? This is a question much research has addressed but remains without a consensus.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Seungwon Shin, Kyung Hee University

Comments to the Author:

The manuscript has been clearly and sufficiently revised.

Thank you, Dr Shin, for your help with the manuscript.

Reviewer: 2

Dr. M Khashram, The University of Auckland Department of Surgery

Comments to the Author:

Thank you again for the opportunity to review the revised manuscript by Dr G Antoniou et al. entitled "Risk factors, risk stratification and risk-specific surveillance strategies after endovascular aneurysm repair: Study protocol of the International Risk Stratification in EVAR (IRIS-EVAR) working group" resubmitted as a protocol for consideration by BMJ Open.

The authors have revised the manuscript and considered the comments and suggestions accordingly. I have no further comments and wish them success with interesting project.

Thank you, Dr Khashram, for your help with the manuscript.

Reviewer: 3

Prof. Alex McConnachie, University of Glasgow

Comments to the Author:

There is very little in the way of statistics for me to comment on, but one thing that struck me was that the "Can't say" responses will be excluded from analyses, which is perfectly fine, but raises the question as to what happens if most people give this response. Is there a threshold for the number or proportion of definite responses that are required?

Many thanks for this comment. We feel it is unlikely that our (generally opinionated) experts would produce a large number of "can't say" responses, hence we did not set a maximum threshold for these. In any case, our protocol calls for the Delphi rounds to be repeated, and in the eventuality consensus cannot be reached (which would be the case if a large number of "can't say" responses are produced), the steering committee will consider the Delphi expert responses and decide on the most appropriate to the survey questions, with an explicit statement that no consensus has been reached, as stated in the Data analysis section of the paper.

Otherwise, my only comment is about the strengths and limitations section of the paper, which lists strengths, but no weaknesses. Surely there are some?

Thank you for the comment. On page 4, we added the following bullet point (number 4): "Risk stratification and risk-informed surveillance strategies will be based on consensus among experts rather than higher levels of evidence; this is an inherent weakness of the study" (page 4, last paragraph).

Reviewer: 4

Dr. Jean Bismuth, Houston Methodist Hospital

Comments to the Author:

Although, I understand the importance of achieving a consensus report on EVAR, as I'm certain the authors are aware, this is a very complex problem with innumerable variables. Its complexity is really the driving obstacle here. I therefore call attention to the issue of selecting experts;

1) The authors underline the need to ensure geographical, sex and age diversity, which is fine, but the complexity of this question is in my opinion linked to several areas of expertise; an explicit understanding of device mechanics, imaging tools (strengths & weaknesses), as well as fluid dynamics. As such it would be beneficial to understand the designation of "experts" in more detail. Thank you, Dr Bismuth, for this comment. We acknowledge that a wide breadth of expertise would be highly beneficial. This is implicit, in our opinion, in the first paragraph of page 8 of the protocol/paper. To this, we added: "The steering committee will focus on inviting experts with a varied clinical and research background, with the intent to include, in particular, individuals with substantial knowledge of the bio-mechanics of the stented aorta" (page 8, 2nd paragraph). There is of course a degree of subjectivity in selecting the areas of expertise of the panel, which will no doubt include imaging, fluid dynamics and device mechanics. It will be the responsibility of the Steering Committee to include experts in these (and other) areas on the basis of a balanced judgement.

2) Given the potential benefits of such a paper, it would be beneficial to understand from the authors how they believe that the work will be able to forecast future solutions and how the work may be used to influence changes at the industry level.

Thank you for the comment. We do not believe that the primary aim of the consensus would be to affect changes at industry level. We hope that wide consensus, assuming this is achieved, could influence current practice until relevant scientific evidence becomes available. We have nevertheless added this statement to the manuscript: "This study will develop a risk stratification instrument, which will help vascular specialists better select the optimal treatment for AAA and tailor post-EVAR surveillance to the individual patient needs (personalised medicine), with the potential of reducing EVAR-related reinterventions, complications, and mortality. We plan to conduct further research aiming to externally validate the ability of the risk stratification tool, that will be developed from the present study, to predict adverse events (reintervention, AAA rupture, and death) after EVAR in a

large population with AAA that have been treated in large tertiary NHS institutions. We believe that our study will pave the way for the development, validation, and application of the risk stratification tool that will be available for use by specialists in the treatment of AAA. Risk stratification will result in individualized (personalised) treatment and follow-up (surveillance) with a direct benefit for patients treated for AAA.” (page 14, lines 1-10).

3) One of the most important elements in this analysis would be to be able to remove all industry bias from this analysis. All clinicians in this arena are tied to primarily one vendor, how is this bias being handled in the analysis? Do the authors feel that this is adequately accounted for?

Thank you for the question. We acknowledge the fact that no clinician is entirely free from industry bias. This bias is impossible to remove from individuals but its effects can be reduced by using large expert panels, as we did in our protocol. Information on conflict of interest will be obtained from steering committee members and Delphi panel participants, and potential conflicts of interest will be dealt with by re-assigning functions or replacing participants who pose interest conflict, as stated in the Ethics and Dissemination section of the manuscript.

4) Have the authors considered also having a question for operative embolization of IMA/Lumbar branches? This is a question much research has addressed but remains without a consensus.

Thank you for the question. We did not ask directly a question on operative side-branch embolization because this technique is rarely, if ever, used in routine practice. We did however address the potential importance of patent side-branches in our protocol. For example (appendix 1): “Is “>2 patent lumbar arteries plus non-patent IMA or >1 patent lumbar artery plus patent IMA” an important predictor of adverse events after EVAR that should be considered in risk stratification and surveillance strategies?”. Further, we will ask (again in appendix I): “Would you suggest any other preoperative anatomy-related predictors of adverse outcomes after EVAR?” and “Is “endoleak (type II)” an important predictor of adverse events after EVAR that should be considered in risk stratification and surveillance strateies?”. These questions should give our panellist ample opportunity to address this issue, albeit indirectly.

VERSION 2 – REVIEW

REVIEWER	McConnachie, Alex University of Glasgow, Robertson Centre for Biostatistics
REVIEW RETURNED	18-Nov-2021

GENERAL COMMENTS	I am happy with the authors responses to my original comments
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